

Applicants: Andrzej Lipkowski et al.  
Serial No.: 10/524,343(a §371 of PCT PCT/PL2003/000077)  
Filed : January 30, 2006  
Page : 8 of 12

#### **REMARKS**

Claims 2-3, 5-9 are pending in the subject application with claims 11-16 withdrawn from consideration. By this Amendment, applicants have amended claim 2. Support for the Amendments to claim 2 can be found in Fig. 2. In addition, applicants have replaced the current Abstract and amended the format of the Brief Description of the Figures. Applicants respectfully request entry of this Amendment. After entry of this Amendment, claims 2-3, 5-9 will be pending in the subject application.

#### **Abstract**

The Examiner objected to the Abstract as failing to disclose the claimed compounds and compositions.

In response, applicants have hereinabove amended the Abstract.

#### **Specification**

The Examiner objected to the description of the figures.

In response, applicants have hereinabove amended the Brief Description of the Figures.

#### **Claim Objections**

The Examiner objected to claims 2, 3 and 5-9 for reciting (Tyr-D-Asn-Gly-Phe-NH-)<sub>2</sub> twice.

Applicants: Andrzej Lipkowski et al.  
Serial No.: 10/524,343(a §371 of PCT PCT/PL2003/000077)  
Filed : January 30, 2006  
Page : 9 of 12

In response, applicants have hereinabove amended claim 2, from which the remaining rejected claims depend, to recite only a single occurrence of "(Tyr-D-Asn-Gly-Phe-NH-)<sub>2</sub>".

**Claims Rejected Under 35 U.S.C. §112, Second Paragraph**

The Examiner objected to claims 2, 3 and 5-9 under 35 U.S.C. §112, second paragraph as being incomplete for omitting essential structural cooperative relationships of elements. The Examiner noted that the rejection could be overcome by amending claim 2 to include Fig. 1 or Fig. 2.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claim 2 to recite, inter alia, the structure shown in Fig. 2. Applicants maintain that, as amended, claim 2, from which the remaining rejected claims depend, is not indefinite and therefore respectfully request that the Examiner reconsider and withdraw this ground of rejection.

**Claims Rejected Under 35 U.S.C. §103(a)**

**Claims 2,3 and 6-8**

The Examiner rejected claims 2, 3 and 6-8 under 35 U.S.C. §103(a) as allegedly obvious over Ronai et al. (*Biochem. Biophys. Res. Comm.*, 1979, 91:1239-1249) in view of Abbruscato et al. (*J. Neurochem.*, 1997, 69:1236-1245) and Kanai et al. (*J. Biol. Chem.*,

Applicants: Andrzej Lipkowski et al.  
Serial No.: 10/524,343(a §371 of PCT PCT/PL2003/000077)  
Filed : January 30, 2006  
Page : 10 of 12

1998, 273:23629-23632). The Examiner asserted that it would have been obvious to one of skill in the art, in light of Kanai et al., to substitute methionine for the alanine in biphalin taught by Abbruscato et al. in order to mimic the tetrapeptide taught by Ronai et al.

In response, applicants respectfully traverse the Examiner's rejection. Applicants initially note that Ronai et al. does not teach a compound comprising two peptides linked by a hydrazine bridge at their C-termini, and instead teaches that any alteration of the C-terminus (of the peptides disclosed therein) "drastically" alters their binding ability (see, e.g., page 1245). In view of this unpredictability, one of ordinary skill in the art, in light of the combination of Ronai et al., Kanai et al. and Abbruscato et al., would have no reasonable expectation of success of the claimed composition which possesses a considerable alteration of the C-terminus.

In addition, applicants note that Kanai et al. has been cited for motivation to change the D-Alanine of the peptide taught by Abbruscato et al. to a D-Methionine in view of Kanai's alleged teaching that the "large neutral amino acid has affinity for methionine". However, Kanai et al. teaches that the transporter is inhibited by the isomer D-Methionine (see Fig. 2c, page 23631). Thus, one of ordinary skill in the art would not be motivated to replace the D-Alanine of the peptide taught by Abbruscato et al. with a D-Methionine. In addition, in view of the transport described in Abbruscato et al., there is no reasonable expectation that the peptide comprising the D-

Applicants: Andrzej Lipkowski et al.  
Serial No.: 10/524,343(a §371 of PCT PCT/PL2003/000077)  
Filed : January 30, 2006  
Page : 11 of 12

Methionine would be an analgesic peptide, i.e. no reasonable expectation of success.

Applicants thus maintain that the compound as claimed is not obvious over the combination of cited art. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims 2,3 and 5-9

The Examiner rejected claims 2, 3 and 5-9 under 35 U.S.C. §103(a) as allegedly obvious over Ronai et al. (*Biochem. Biophys. Res. Comm.*, 1979, 91:1239-1249) in view of Abbruscato et al. (*J. Neurochem.*, 1997, 69:1236-1245) and Kanai et al. (*J. Biol. Chem.*, 1998, 273:23629-23632) in further view of Hill et al. (U.S. Patent No. 5,880,132), Bock et al. (EP 0434369) and Ornstein (U.S. Patent No. 5,356,902). The Examiner asserted that Ornstein, Hill and Bock et al. teach stimulatory amino acids, tachykinins and cholecystokinin receptor antagonists, and that Abbruscato et al. teaches biphalin, and that it would have been obvious to one of skill in the art to combine the teachings of the cited art to arrive at the invention as claimed.

In response, applicants respectfully traverse the Examiner's rejection. Applicants have stated hereinabove why the invention as claimed is not obvious over the combination of Ronai et al., Abbruscato et al., and Kanai et al. Applicants further note that the teachings of Hill et al., Bock et al. and Ornstein, in combination with the remaining cited art, do not cure this deficiency. The combination of references does not teach or

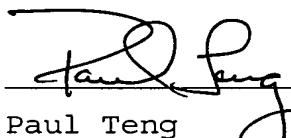
Applicants: Andrzej Lipkowski et al.  
Serial No.: 10/524,343(a \$371 of PCT PCT/PL2003/000077)  
Filed : January 30, 2006  
Page : 12 of 12

suggest (Tyr-D-Met-Gly-Phe-NH-)<sub>2</sub>, and does not teach or suggest applicants' invention. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

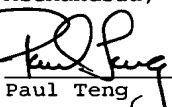
If a telephone interview would be of assistance in advancing prosecution of the subject application, the undersigned attorneys invite the Examiner to telephone them at the telephone number provided below.

No fee, apart from the enclosed \$60.00 fee for a one-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



Paul Teng  
Registration No. 40,837  
Gary J. Gershik  
Registration No. 39,992  
Attorneys for Applicant  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	
 Paul Teng Reg. No. 40,837	<u>October 26, 2007</u> Date